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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/425,956	10/25/1999	RUDOLPH E. TANZI	0609.4110001	1225

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EXAMINER
DUFFY, PATRICIA ANN

ART UNIT	PAPER NUMBER
1645	15

DATE MAILED: 05/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/425,956	Tanzi et al
Examiner	**Art Unit**
Patricia A. Duffy	1645

FILE COPY

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *amendments 2-27-02* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above, claim(s) *31-34* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-30* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *1-34* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *4*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Response to Amendment

1. The amendment filed 2-27-02 has been entered into the record. Claims 1-34 are pending and under examination.

2. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

3. Any rejection not reiterated herein is withdrawn based on Applicants' amendments.

Objections/Rejections Maintained

Drawings

4. This application has been filed with informal drawings which are acceptable for examination purposes only. The drawings are objected to by the draftsperson under 37 C.F.R. 1.84 or 1.152. See PTO-948 for details. Correction of the noted defects can be deferred until the application is allowed by the examiner.

Election/Restriction

5. This application contains claims 31-34 drawn to an invention nonelected without traverse in Paper No. 7. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Double Patenting

6. The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise

extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel,* 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornum,* 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi,* 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman,* 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) and © may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-16 and newly amended claims 17-30 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 5,972,634. Although the conflicting claims are not identical, they are not patentably distinct from each other because the term "antibody" of the patent is inclusive of both polyclonal and monoclonal antibodies.

Applicants indicate that a terminal disclaimer will be filed upon notice of a allowable subject matter. This is not persuasive, this rejection is not provisional and no allowable subject matter can be indicated until this rejection is overcome.

Claim Rejections - 35 U.S.C. § 112

8. Claims 5-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

For clarification , the rejection is applied to only polyclonal antibodies as claimed that have the recited binding specificity. Since the claims as presented for original examination do not encompass monoclonal antibodies. Applicants comments in the previous case and evidence presented therein were convincing only for monoclonal antibodies. Unlike monoclonal antibodies that bind a single epitope of defined specificity, polyclonal antibodies are a collection of antibodies with disparate and different binding specificities. Unlike polyclonal antibodies, the screening methods for monoclonal antibodies can identify those antibodies with the requisite binding specificity. Further, the art specifically described such monoclonal antibodies at the time of filing of this application. However, the art did not describe such polyclonal antibodies and unlike monoclonal antibodies, the polyclonal antibody is composition or collection of discrete antibodies with individual binding properties. Applicants now submit a Declaration by Dr. Richard Strungell pursuant to 37 CFR 1.132 to traverse this rejection to support applicants contention that only routine experimentation would be required to make polyclonal antibodies with the claimed

binding specificity. The declaration of Dr. Strungell has been carefully considered but is not persuasive. First, in Point 9, Dr. Strungell acknowledges that one would have recognized that in order to produce a polyclonal antibody specific for each peptide it would be necessary to select an appropriate immunogen bearing these respective unique epitopes. It is noted that these unique immunogens are not described by this specification. As previously set forth, the courts have held that "... whenever there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of the invention in order to constitute adequate enablement." *Genetech Inc. v. Novo Nordisk A/S* 42USPQ2d 1001. As in Genetech, the art does not describe an immunogen with the ability to produce a monoclonal antibody with the claimed binding properties. As to point 10, applicants allege that it is common to generate antibodies that are capable of distinguishing between closely related molecules and cites Geysen et al. It is noted that Geysen et al provides no teaching of polyclonal antibodies that bind as claimed. Geysen et al provides for epitope mapping and studies the binding of polyclonal antibodies to subsequence and some variants of the

natural sequence (see Table 1, page 4000) and is not directed to using peptides or immunogens to produce polyclonal antibodies that bind one sequence but not another as is specifically claimed.. It is noted that the claims are not variants and do not provide for the extensive epitope mapping studies provided by Geysen et al for the immunodominant eiptope of a virus. Geysen et al is not seen to teach the missing element of the specification, the immunogen that predictably and reproducibly provides for a polyclonal antibody with the claimed binding pattern, and Declarant acknowledges this as not provided asserting that its determination is routine skill in the art. Applicants points 10 and 11 indicate that peptide epitopes could be resolved using extensive technology and techniques not taught in this specification. Moreover, Xing et al supports the examiners position in stating that "Within (S)APDTR, major amino acids substitutions could be made -- even three to four amino acids without altering antibody binding, provided that P and R were not substituted." (see abstract page 641). Thus, extensive studies are necessary to determine critical antibody binding epitopes with respect to the binding specificity of a monoclonal antibody. It is noted that many epitope mapping studies relied upon by Declarant, are performed using monoclonal antibodies. Clear differences exist between monoclonal and polyclonal antibodies exist when the antibodies are generated using the same immunogen. Take for example the peptide (S)APDTR of Xing et al. While one

specific monoclonal antibody may have the specificity of requiring P and R to be present, the same peptide when used as an immunogen to produce a polyclonal antibody will have multiple specificities, because the polyclonal antibody is in fact a collection of monoclonal antibodies each with different specificities. The polyclonal antibody that acts as a collection can not and does not discriminate between variant as asserted by applicants. Therefore, the discrimination of polyclonal antibodies with respect to that generated to the peptide of (S)APDTR is not provided by the teachings of Xing et al. Declarant asserts that thes knowledge of the prior art would lead to a proper immunogen. This is the critical starting material for the production of polyclonal antisera with the claimed binding specificity that is not taught by this specification. From Applicants declaration it is clear that extensive experimentation must be performed to identify the appropriate immunogen that might possibly produce a polyclonal antibody with the claimed binding specificity. Declarant proposes that all the information for the production of polyclonal antibodies with the requisite binding specificity is in the art. The examiner disagrees, the immunogen to produce the polyclonal antibody is the criticality upon which the production of the polyclonal antibody having the specifically claimed binding properties is based. This specific immunogen is not known to the art with respect to the production of polyclonal antibodies and is not taught by applicants. As such, the immunogen, the critical element of

the routine method of making polyclonal antibodies is not provided by way of written description in this specification. Absent written description of such an immunogen, this specification clearly fails to provide enablement of how to make and use polyclonal antibodies of the claimed binding specificity. Failure to disclose the critical immunogen for the production of polyclonal antibodies with specific binding properties for use in the methods and kits as now claimed is not overcome by the Expert Declaration of Dr. Strungell that asserts that all the skill to produce such is in the art and is therefore not persuasive. Declarant's position that one skilled in the art could discover the appropriate immunogen and ascertain appropriate binding assays is not persuasive because such acts are part of the act of invention. The examiner maintains that in absence of the written description of the appropriate immunogen in the specification as originally filed, that the production of polyclonal antibodies with the requisite binding specificity are not enabled by this specification. Declarant acknowledges that the appropriate immunogen is not described herein, but the skill in the art allows one to discover such. These arguments as set forth by Declarant's are not persuasive because the written description of the specification must enable one skilled in the art to make and use the reagents as required by the method and this fundamental requirement of 112, first paragraph, thatcan not be overcome by asserting that the skill in the art enables one to make such. As set forth

herein and in the previous office action, this specification does not provide a written description of how to make such, because it clearly lacks written description of the appropriate immunogen that makes the claimed polyclonal antibodies with the appropriate binding specificity.

The rejection is maintained.

Status of Claims

9. All claims stand rejected.

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action with respect to obvious double patenting. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

11. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Thursday and Saturday from 10:30 AM to 7:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached at (703) 308-3909.

Patricia A. Duffy, Ph.D.
May 18, 2002

Patricia A. Duffy, Ph.D.
Primary Examiner
Group 1600